Long Term Results of non-penetrating Deep Sclerectomy with Esnoper V-2000 Implant in a Tertiary Center of Ophthalmology

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ABSTRACT

Introduction: Nonpenetrating deep sclerectomy (NPDS) is one of the surgical procedures used for lowering intraocular pressure (IOP) in patients with uncontrolled open-angle glaucoma. This surgery can be enhanced with the use of antimetabolites as well as implants - devices that are placed to facilitate the aqueous outflow by maintaining the virtual space created after removing the deep scleral flap. The purpose of this study was to report the long-term efficacy and safety of NPDS with adjunctive mitomycin C (MMC) and a nonabsorbable hydroxyethyl methacrylate implant (Esnoper V-2000) in our institution.

Methods: This is a retrospective study. Inclusion criteria were: NPDS with adjunctive use of MMC and Esnoper V2000 and follow-up time post-NPDS≥24 months. Of 55 NPDS surgeries performed between April 2013 and January 2017 in our institution, 41 eyes (37 patients) met the inclusion criteria. Primary outcome was surgical success, defined as IOP≤18mmHg and IOP reduction rate (IOP-RR)≥20%, either with (relative) or without (absolute) need of IOP-lowering drugs, and without additional surgery. Secondary outcomes were percentage of patients with IOP≤14mmHg at 2 years and last follow-up, change in number of antihypertensive drugs, Nd:YAG goniopuncture (Nd:YAG GP) rate, and need for additional glaucoma surgery.

Results: Mean patient age at NPDS was 68.78 (±11.26) years. Median pre-NPDS IOP was 22 (7.0) mmHg on median of 4 (1) IOP-lowering drugs. Mean follow-up time post-NPDS was 41.54 (±13.41) months. Median IOP at 24 months was 14.0 (6.5) mmHg and, at last-follow-up, was 15.0 (6.0), both on a median number of 1 (2) IOP-lowering drugs. Statistically significant reductions in median IOP and IOP-lowering drugs were observed at 24 months and at last follow-up compared to baseline ($p<0.001$). Success rate at 24 months was 58.5% (24.4% relative + 34.1% absolute success) and 53.7% at last follow-up (29.3% relative + 24.4% absolute success). Nd:YAG GP rate was 39%, performed at a mean time of 13.25 (±6.8) months post-NPDS. Four eyes (9.8%) needed additional glaucoma surgery.

Conclusions: In our study, NPDS with adjunctive MMC and Esnoper V-2000 resulted in a significant reduction in IOP and number of IOP-lowering drugs over the long term, with a relatively high surgical success rate. Our patients could possibly benefit from a higher rate of Nd:YAG GP which was lower than reported in other studies.

RESUMO

Introdução: A esclerectomia profunda não penetrante (EPNP) é um dos procedimentos cirúrgicos utilizados para diminuir a pressão intra-ocular (PIO) em doentes com glaucoma de ângulo aberto não controlado. Esta cirurgia pode ser melhorada com o uso de antimetablitos assim como de implantes - dispositivos colocados para facilitar a drenagem do humor aquoso ao manter o espaço virtual criado após remover o flap escleral profundo. O objetivo deste estudo é avaliar a eficácia e segurança a longo prazo da EPNP com uso adjuvante de mitomicina C (MMC) e do dispositivo de hidroxietil metacrilato não absorvível (Esnoper V-2000) na nossa instituição.

Métodos: Este é um estudo retrospectivo. Os critérios de inclusão foram: utilização de MMC e Esnoper V-2000 adjuvantes e seguimento pós-EPNP≥24 meses. Das 55 cirurgias realizadas entre Abril de 2013 e Janeiro de 2017 na nossa instituição, 41 olhos (37 doentes) cumpriam os critérios de inclusão. Os resultados primários avaliados foram o sucesso cirúrgico, definido como PIO≤18mmHg e taxa de redução da PIO (IOP-RR)≥20%, com (relativo) ou sem (absoluto) necessidade de fármacos antiglaucomatosos e sem cirurgia adicional. Os resultados secundários que foram avaliados foram percentagem de doentes com PIO≤14mmHg aos 2 anos e última consulta, a alteração do número de fármacos antiglaucomatosos; a taxa de goniopunção por Nd:YAG (Nd:YAG GP) e a necessidade de cirurgia adicional.

Resultados: A idade média dos doentes foi de 68.78 (±11.26) anos. A PIO pré-EPNP mediana era de 22 (7.0) mmHg numa mediana de 4 (1) fármacos anti-glaucomatosos. O tempo de seguimento médio pós EPNP foi de 41.54 (±13.41) meses. A PIO mediana aos 24 meses foi de 14.0 (6.5) mmHg e na última consulta de 15 (6) mmHg, ambos com mediana de 1 (2) fármaco anti-glaucomatoso. Aos 24 meses e na última consulta foram observadas diminuições estatisticamente significativas na PIO mediana e no número de fármacos anti-glaucomatosos em comparação com a linha de base ($p<0.001$). A taxa de sucesso aos 24 meses foi de 58.5% (24.4% sucesso relativo + 34.1% absoluto) e na última consulta foi de 53.7% (29.3% sucesso relativo + 24.4% absoluto). A taxa de Nd:YAG GP foi 39%, realizada um tempo médio de 13.25 (±6.8) meses pós-EPNP. Quatro olhos (9.8%) necessitaram de cirurgia adicional.

Conclusão: Neste estudo, a EPNP com MMC e Esnoper V-2000 resultou numa diminuição significativa da PIO e do número de fármacos antiglaucomatosos a longo prazo, com uma taxa de sucesso relativamente alta. Os nossos doentes poderiam beneficiar de uma taxa de Nd:YAG mais elevada, que no nosso caso foi mais baixa do que noutros estudos.

INTRODUCTION

Nonpenetrating deep sclerectomy (NPDS) is one of the surgical procedures used for lowering intraocular pressure (IOP) in patients with uncontrolled open-angle glaucoma (OAG).[1] It works by creating a new pathway for the outflow of the aqueous humour (AH) while keeping the integrity of the anterior chamber (AC) intact.[2] It is created an intrascleral space separated from the AC by a thin membrane formed by the trabecular meshwork and Descemet's membrane (TDM). From this location, the AH is drained via three routs: subconjunctival, intrascleral and suprachoroidal.[1] This surgery can be enhanced with the use of antimetabolites, such as mitomycin C (MMC) or 5-fluorouracil, as well as implants, which are devices placed to facilitate the aqueous outflow by maintaining the virtual space created after removing the deep scleral flap.[3] The purpose of this study was to report the long-term efficacy and safety of non-penetrating deep sclerectomy (NPDS) with adjunctive mitomycin C (MMC) and the nonabsorbable hydroxyethyl methacrylate (HEMA) implant Esnoper V-2000 (Esnoper®, AJL Ophthalmics, SA, Minano, Alava, Spain)[1] in our institution.

METHODS

It is a retrospective hospital-based study. We selected all eyes in which NPDS with adjunctive use of MMC and Esnoper V-2000 was performed, between April 2013 and January 2017 and that had a follow-up time post-NPDS≥24 months. They didn't have any history of previous glaucoma surgery.

Of the 55 NPDS surgeries performed in this period in our institution, 41 eyes (37 patients) met the inclusion criteria. The primary outcome was surgical success, defined as IOP at last follow-up observation ≤18mmHg and IOP reduction rate (IOP-RR) ≥20%, either with (relative) or without (absolute) need of IOP-lowering drugs, and without additional surgery. Secondary outcomes were percentage of patients with IOP≤14mmHg at 2 years and last follow-up, change in the number of antihypertensive drugs, Nd:YAG goniopuncture (Nd:YAG GP) rate, and need for additional glaucoma surgery after 24 months of follow-up.

Data are presented as "mean ± standard deviation" for normal distribution samples or "median (interquartile range)" when the distribution is not normal. All statistical analyses were performed using SPSS statistical software (SPSS, Inc., Chicago, IL, USA). Non-parametric Wilcoxon test was used to evaluate between and within-group differences. A p value of 0.01 or less was considered statistically significant.

RESULTS

Mean patient age at NPDS was 68.78 (±11.26) years, 25 were males and 16 females. About the operated eyes, 20 were right and 21 left eyes. 61% had the diagnosis of primary open angle glaucoma (POAG); 29,3% pseudoexfoliative glaucoma (PXG); 4,9% pigmentary dispersion glaucoma (PDG) and 4,9% inflammatory glaucoma. 70,7% of patients had a simple NPDS and the remaining 29,3% had a combined NPDS surgery with phacoemulsification. Mean follow-up time post-NPDS was 41.54 (±13.41) months.

n	**41**
Age (years)	68.78 (±11.26)
Sex (Male / Female)	(25 / 16)
Laterality	
OD	20
OS	21
Type of Glaucoma	
POAG	25 (61,0%)
PXG	12 (29,3%)
PDG	2 (4,9%)
Inflammatory	2 (4,9%)
Type of surgery	
NPDS	29 (70,7%)
Combined (Phaco + NPDS)	12 (29,3%)
Follow-up time (months)	41,54 (±13.41)

Table 1 - Clinical and demographic characteristics of patients included in this study

Median pre-NPDS IOP was 22 (7.0) mmHg on a median of 4 (1) IOP-lowering drugs. Median IOP at 2 years of follow-up was 14.00 (6.5) mmHg on a median of 1 (2) IOP-lowering drugs. Median IOP at last follow-up was 15.00 (6.0) mmHg on a median of 1 (2) IOP-lowering drugs. The IOP was ≤14mmHg in 51,2% of the patients at 2 years and 46,3% at last-follow-up. Statistically significant reductions in median IOP were observed at 2-years and at last follow-up compared to baseline ($p<0.01$). At last follow-up, the IOP was not statistically different from any other point of the follow-up ($p>0.01$). There is also a statistical difference between the number of IOP-lowering drugs pre-NPDS and at 2-years ($p<0,01$) and also between the number of IOP-lowering drugs pre-NPDS and at last follow-up post-NPDS ($p<0,01$).

Success rate at 2-years was 58.5% (24.4% relative + 34.1% absolute success). At last follow-up the success rate

was 53.7% (29.3% relative + 24.4% absolute success). There was no difference in the success rate between POAG and PXG patients.

IOP	Median	IQR
Pre-NPDS	22,00	7,00
1M post-NPDS	14,50	6,00
6M post-NPDS	14,00	5,25
1Y post-NPDS	14,00	6,00
2Y post-NPDS	14,00	6,50
At last follow-up	15,00	6,00

Table 2 - IOP variation

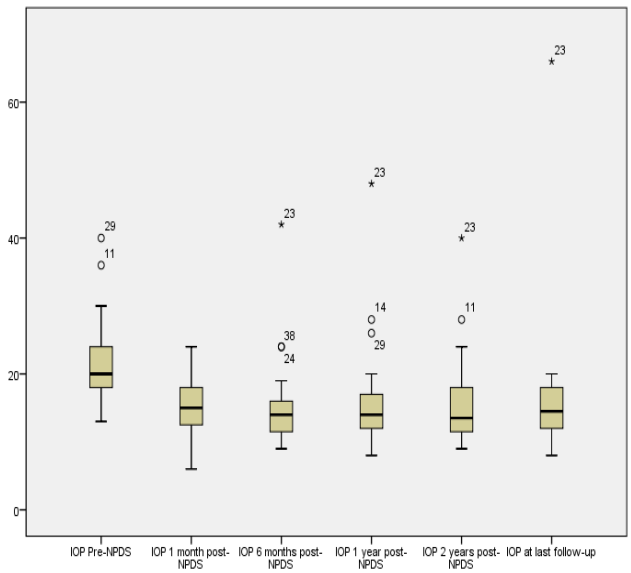

Figure 1 - IOP variation through follow-up. There was a statistically significant decrease in IOP in each time-point of follow-up in comparison with the pre-NPDS IOP ($p<0.01$).

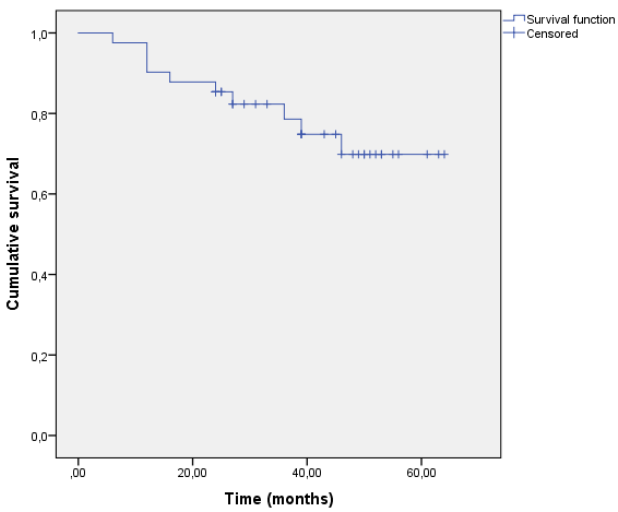

Figure 2 - Kaplan Meier curve. It represents the percentage of patients that had IOP≤18mmHg throughout follow-up. The vertical lines represent the patients who still had IOP≤18mmHg at last-follow-up.

Follow-up time	Not successful	Success		
		Relative	Absolut	Total
2Y post-NPDS	17 (41,5%)	10 (24,4%)	14 (34,1%)	24 (58,5%)
At last follow-up	19 (43,6%)	12 (29,3%)	10 (24,4%)	22 (53,7%)

Table 3 - Success Rate

Goniopuncture rate was 39%, performed at a mean time of 13.25 (±6.8) months post-NPDS. Four eyes (9.8%) needed additional glaucoma surgery, 2 of them before 24 months of follow-up and the other 2 after the 24 months of follow-up.

As long-term complications we had one patient who had an Irvine-Gass syndrome after Nd:YAG GP at 27 months follow-up. This same patient had a blunt trauma with hyphema 3 years post-NPDS. A second patient had a post-traumatic hypotonia 30 months post-NPDS.

DISCUSSION

We had a significant reduction of IOP from a median of 22 (7) mmHg to a median of 14 (6.5) mmHg, which was similar to other studies with 1 or 2 years of follow-up that used the same implant.[1,3] We also had a significant reduction in the number of glaucoma drugs and a low rate of long-term complications.

The total success rate (absolute + relative) was 58,5% at 2 years of follow-up and 53,7% at last follow-up, what is less than we were expecting regarding another study that defined success with the same criteria but used Esnoper-Clip.[4] Our glaucoma service is a reference centre for glaucoma surgery. This is a retrospective study and so, it is possible that some of the excluded patients had a well-controlled IOP and were sent back to the origin centre before the 24 months post-NPDS to keep the follow-up there. This could have created a bias (if the excluded patients had better results than the ones included) with lower success rates than other studies.

Nd:YAG GP improves long-term surgical success due to the microperforation of the TDM and the subsequent increase of aqueous outflow. It is a noninvasive, quick, and inexpensive procedure.[2] It has been noticed that the need for Nd:YAG GP increases with longer follow-up after NPDS to achieve a within target IOP range.[5] In our study we verified that the number of topical glaucoma drugs at 2 years follow-up (median of 1) was high and the

number of patients who had Nd:YAG GP was low (39%) when in comparison with other studies. *Loscos-Arenas et al*[3] had a mean number of glaucoma drugs of 0,4 at 2 years post NPDS and performed Nd:YAG GP on 62,5% of their patients after NPDS with MMC and Esnoper V-2000. In our service we had a period in which the Nd:YAG machine was inoperable, and so, many patients that could have benefitted from goniopuncture, were instead started on IOP-lowering drugs, which diminished our absolute success rate.

The majority of our patients was under maximal medical therapy before surgery. Many were operated not only to stop progression but also to diminish the topical drugs burden. In these cases, the pre-NPDS IOP with glaucoma drugs may not be very different from the post-op IOP without drugs and the IOP-RR is not ≥20%, so the surgery is considered not successful by our criteria. Regarding these cases, the success criteria used may be too exigent, excluding patients who benefitted a lot from the surgery. If we exclude the IOP-RR from our criteria and consider only IOP≤18mmHg, we have a surgical success of 75,6% (29,3% absolute + 46,3% relative) and only 24,4% of not successful cases at last follow-up.

There was no difference in the success rate between POAG and PXG patients. Even though some studies concluded that NPDS in inflammatory glaucoma is efficacious and has few postoperative complications,[6] the only 2 patients in our study with this diagnostic were not successful.

In conclusion, in our institution, NPDS with adjunctive MMC and Esnoper V-2000 was a safe procedure that resulted in a significant reduction in IOP and number of IOP-lowering drugs over the long term, with a relatively high surgical success rate. Our patients could possibly benefit from a higher rate of Nd:YAG GP.

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Conflicts of Interest
The authors declare that there are no conflicts of interest regarding the publication of this article.